Research Article
Volume 15:2, 2025

Journal of Nephrology & Therapeutics

ISSN: 2161-0959 Open Access

Impact of Catheter Lock Solutions and Patient Factors on Catheter Colonization in Temporary Hemodialysis Catheters

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Abstract

Objective: This study aimed to investigate the impact of catheter lock solutions in hemodialysis catheters on colonization and explore other factors influencing colonization.

Methods: A total of 73 consecutive patients were prospectively included in the study. Demographic data, etiology, catheter insertion site, number of hemodialysis sessions, duration of catheter use, and history of coronary artery disease, anticoagulant, and antilipidemic drug usage were recorded. Nasal cultures were obtained, and patients were divided into two groups based on the catheter lock solutions used: heparin and 30% trisodium citrate. The frequency of colonization, culture results, and factors affecting colonization were compared between the two solution groups.

Results: A total of 67 catheters were inserted in 59 patients. The mean follow-up duration was 25.4 ± 27.02 (7-113) days, and the mean number of hemodialysis sessions was 10.9 ± 10.8 (2-46) times. Thirty-two catheters in 29 patients were closed with heparin, while 35 catheters in 30 patients were closed with citrate. The heparin group had a longer catheter duration and a higher number of dialysis sessions compared to the citrate group ($p<0.005$ for both). The presence of systemic infections and nasal carriage was similar between the two groups ($p>0.005$ for both). The culture positivity rate was 34% in the heparin group and 23% in the citrate group (p: 0.46). The infection rate was higher in jugular catheters closed with heparin and femoral catheters closed with citrate. A significant correlation was observed between catheter tip colonization and a history of infection in the heparin group (r: 0.405, p: 0.02), and between colonization and catheter localization in the citrate group (r: 0.440, p: 0.008).

Conclusion: Catheter lock solutions did not have a significant effect on the frequency of catheter colonization. The site of catheter insertion, duration of catheter use, and systemic infectious status were identified as factors influencing catheter colonization in temporary hemodialysis catheters.

Keywords: Catheter lock solutions • Catheter colonization • Hemodialysis catheters • Infectious complications • Catheter-related infections

Introduction

Vascular access plays a crucial role in hemodialysis for patients, with various methods employed including catheters with or without a tunnel, Arteriovenous Fistula (AVF), and synthetic or biologic grafts (AVG). However, these access routes can give rise to complications that significantly impact the well-being and survival rates of hemodialysis patients [1]. Among the numerous complications faced by individuals with renal failure, infections stand out as one of the leading causes

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Received: 27 October, 2023, Manuscript No. JNT-23-118540; **Editor assigned:** 30 October, 2023, PreQC No. JNT-23-118540 (PQ); **Reviewed:** 15 November, 2023, QC No. JNT-23-118540; **Revised:** 03 March, 2025, Manuscript No. JNT-23-118540 (R); **Published:** 10 March, 2025, DOI: 10.37421/2161-0959.2025.15.552

of mortality [3-5]. Remarkably, over 70% of infections in hemodialysis patients are associated with the vascular access site, and the utilization of hemodialysis catheters is frequently responsible for bacteremia in these cases [5-7]. It is believed that catheter-related infections occur through distinct mechanisms, beginning with contamination of the catheter hub, followed by colonization of the catheter and subsequent formation of bacterial biofilm on its inner and outer surfaces. This process is considered a major pathway for catheter-related infections and the development of thrombosis within the catheter lumen [7-9]. Particularly, the primary source of Catheter-Related Bacteremia (CRB) is the microbial biofilm layer that forms at the subcutaneous part of the catheter insertion. Preventing the formation of this biofilm layer is crucial for reducing CRB incidence. In vitro studies have demonstrated the efficacy of implementing antibiotics at supraphysiological concentrations against microorganisms in the tunnel. Furthermore, non-antibiotic antimicrobial agents, such as taurolidine, 30% citrate, and 70% ethanol, have exhibited broad-spectrum bactericidal activity under *in vitro* conditions [10].

Furthermore, in the context of catheter closure, concentrated heparin is commonly employed; however, the use of heparin may lead to bleeding complications [11]. Conversely, Trisodium Citrate (TSC) has been reported to chelate calcium and magnesium, thereby influencing bacterial growth, preventing biofilm formation, and impeding bacterial colonization [12-14]. The objective of this study was to investigate the impact of two different catheter lock solutions on catheter colonization, as well as the factors that may influence colonization, in patients undergoing hemodialysis with temporary hemodialysis catheters.

Materials and Methods

This study was conducted at the Hemodialysis Unit of the Clinic of Nephrology in Sisli Etfal Education and Research Hospital. Between February 2011 and July 2011, a total of 73 consecutive patients diagnosed with Acute Renal Failure (ARF) or End-Stage Renal Disease (ESRD) underwent the immediate insertion of temporary hemodialysis catheters to facilitate hemodialysis. These patients were prospectively enrolled in the study. Nephrology specialists or nephrology fellows performed the placement of a total of 89 temporary hemodialysis catheters using a blind technique assisted by a guide. Patients who experienced mortality, were transferred to the intensive care unit, or were referred to other dialysis centers resulting in catheter removal were excluded from the study.

Catheter insertion

In our unit, temporary hemodialysis catheters were predominantly inserted in patients *via* the right internal jugular vein or femoral vein, while subclavian vein catheterization was not commonly employed. The catheter placements were carried out in a sterile environment using local anesthesia and a blind technique, without the assistance of ultrasound guidance. Prior to each dialysis session, patients with jugular catheters underwent evaluation with (PA) chest radiographs to ensure correct positioning and to monitor for potential complications such as hemothorax or pneumothorax that may arise during the insertion procedure.

Catheters

The catheters utilized in this study were double-lumen polyurethane catheters with a seal. The specific diameter and length of the catheters varied depending on the site of insertion. Throughout the study period, jugular catheters measuring 12 cm in length and 11.5 French (F) in diameter (Medcomp XTP114IJS, Harleysville, PA, USA) and femoral catheters measuring 15 cm in length and 12 F in diameter (Medcomp XTP126MT, Harleysville, PA, USA) were inserted in the patients.

Procedures

Catheters were exclusively used for hemodialysis purposes and not for any other functions. Before each hemodialysis procedure, infection control measures were implemented, and the catheter insertion site was covered with a povidone-iodine dressing. After the dialysis session, the catheter lumens were flushed with 0.9% sodium chloride. Subsequently, the catheters were closed with an amount of closure solution (sodium heparin at a concentration of 5000 IU/ml or a 30% concentration of trisodium citrate) matching the volume of the catheter lumen, ensuring it did not escape into the systemic circulation. Prior to the initiation of the next dialysis session, any remaining solution in the lumen was aspirated, and then hemodialysis was initiated. This process continued until the catheter was removed for any reason. Patients who required catheter replacement received new catheters closed with the same closure solutions and were not excluded from the study. Elective removal of catheters occurred when the need for dialysis was no longer present in cases of acute renal failure, when hemodialysis continued through Arteriovenous Fistula (AVF), Arteriovenous Graft (AVG), or permanent catheters in End-Stage Renal Disease (ESRD). Catheters were immediately removed in situations where there was a high probability of catheter infection, such as erythema and/or purulent drainage at the catheter site. In patients with femoral catheters, if Deep Vein Thrombosis (DVT) was detected in the same extremity as the catheter confirmed by venous Doppler ultrasound, the catheters were promptly removed. A 3-4 cm segment from the tip of all removed catheters was cut using sterile scissors and placed in sterile containers for culture analysis in the laboratory.

Data collection

Each patient's demographic data (age, gender, Body Mass Index (BMI)), disease etiology, catheter insertion site, closure solution type, number of hemodialysis sessions, and duration of catheter use were recorded. Patients were also questioned about their history of coronary artery disease and the use of anticoagulant drugs (such as acetylsalicylic acid, warfarin, or low molecular weight heparin) and

anti-lipemic drugs. Pre-dialysis complete blood count, serum urea, creatinine, albumin, fibrinogen, and C-Reactive Protein (CRP) levels were measured for all patients. Complete blood count and CRP were also reassessed during catheter removal. Nasal cultures were obtained from patients to assess nasal carriage during the first dialysis session. The patients were divided into two groups based on the type of catheter lock solutions used: Heparin and Trisodium Citrate (TSC). The frequency of catheter colonization, microorganisms isolated from the cultures, and factors that potentially influenced colonization were compared between the two groups.

Statistical analysis

Statistical analysis was conducted using SPSS 17.0 (SPSS Inc., USA) software. The data were presented as mean and standard deviation. Student's t-test was employed to compare continuous variables, while the *chi-square* test was used for categorical variables. Pearson and Spearman tests were utilized for correlation analysis. A significance level of $P<0.05$ was considered statistically significant.

Results

Patient demographics and catheter characteristics

During the study period, a total of 89 temporary hemodialysis catheters were used for 73 patients. Three patients were transferred to the intensive care unit, 3 patients died, and 8 patients were transferred to another dialysis center, resulting in their exclusion from the study. Ultimately, 67 catheters were inserted in 59 patients. The mean age of the patients was 56.5 ± 17.6 years, with 22 of them being women. In two patients, the catheters were inserted three times, while in four patients, the catheters were inserted twice. All of these catheter insertions involved the removal of the femoral vein catheters and insertion into the right jugular vein. The mean follow-up period for the catheters was 25.4 ± 27.02 days (ranging from 7 to 113 days), and the mean number of hemodialysis sessions was 10.9 ± 10.8 sessions (ranging from 2 to 46 sessions). Fifteen patients had catheters inserted due to Acute Renal Failure (ARF), while the remaining 58 patients had catheters inserted due to End-Stage Renal Disease (ESRD). Among the patients with ESRD, the etiology was diabetes mellitus in 21 patients and hypertension in 17 patients. Thirty-one out of the 67 catheter insertions were performed in the right jugular vein, while 36 were performed in the femoral vein.

Comparison of socio-demographic and laboratory data

The catheters were divided into two groups based on the type of catheter lock solutions used: Group 1 consisted of catheters closed with heparin (29 patients), and group 2 consisted of catheters closed with 30% TSC (30 patients). The history of systemic infection was present in 3 patients in group 1 and 5 patients in group 2, with no significant difference observed between the groups in terms of infection presence (p=0.71). The socio-demographic and laboratory data of both groups are presented in Tables 1 and 2. The frequency of systemic infections and nasal carriage was similar between the groups (p=0.71, 0.18 respectively). The carriage of Methicillin-Sensitive *Staphylococcus aureus* (MSSA), determined through nasal cultures performed before catheter insertion, was detected in 4 patients in group 1 and 2 patients in group 2 (p=0.18). Among patients with MSSA carriage, MSSA colonization in the catheter was detected in only one patient in group 1 and was not detected in group 2. There was no correlation between nasal carriage and catheter colonization in both groups (r=0.134, p=0.46).

Parameter	Group 1	Group 2	P
Age (years)	57.1 ± 16.2	53.0 ± 19.0	0.19
Gender (M/F)	10/19	12/18	0.94
BMI (kg/m^2)	24.4 ± 4.8	24.9 ± 6.4	0.18
Number of hemodialysis sessions	12.5 ± 13.2	9.5 ± 8.0	0.02
Total catheter follow-up period (days)	31.3 ± 34.0	20.0 ± 18.1	0.003
Jugular catheter follow-up period (days)	48.8 ± 38.6	32.4 ± 20.6	0.007
Femoral catheter follow-up period (days)	11.4 ± 7.2	11.7 ± 10.1	0.59
Presence of coronary artery disease	3	2	0.33
Presence of hyperlipidemia	6	6	0.99
Anticoagulant medication usage	7	3	0.17

Note: Group 1: Catheters closed with heparin. Group 2: Catheters closed with citrate solution. BMI: Body Mass Index

Table 1. Comparative analysis of socio-demographic data between groups.

Parameter	Group 1	Group 2	P
CRP (mg/L)	68.8 ± 97.4	64.5 ± 69.9	0.83
CRP-final (mg/L)	43.2 ± 47.0	50.4 ± 60.3	0.59
WBC (mm^3)	8792.2 ± 4965.1	9356.0 ± 3540.1	0.59
WBC-final (mm^3)	8280.9 ± 3291.1	9354.3 ± 3650.9	0.21
Hb (g/dl)	8.8 ± 1.5	8.6 ± 1.7	0.67
Hb-final (g/dl)	9.1 ± 1.6	9.1 ± 1.7	0.97
Fibrinogen (g/dl)	386.4 ± 137.1	400.2 ± 120.0	0.68
Albumin (g/dl)	3.4 ± 0.6	3.2 ± 0.7	0.24
HbA1c (%)	5.7 ± 1.5	5.3 ± 0.9	0.15
Ca x P	48.9 ± 20.4	57.5 ± 20.2	0.08
PTH (pg/ml)	504.0 ± 381.2	526.0 ± 492.3	0.84

Note: Group 1: Catheters closed with heparin. Group 2: Catheters closed with citrate solution. CRP: C-reactive Protein, WBC: White Blood Cell, Hb: Hemoglobin, PTH: Parathyroid Hormone

Table 2. Comparison of laboratory data between groups.

Catheter colonization and culture results

During the study, the culture results of the catheter tips were positive in 34% of patients (n=11) whose catheters were closed with heparin and in 23% of patients (n=8) whose catheters were closed with citrate solution (p=0.46). The microorganisms obtained from the cultures are presented in Table 3. In group 1, the culture-positive catheters were more frequent in the femoral region (2 patients) compared to the jugular region (9 patients) (p=0.018). In group 2, culture-positive catheters were more frequent in the femoral region (8 patients), while no culture positivity was detected in jugular catheters (n=14) in this group (p=0.012). The infection rate was higher in jugular catheters closed with heparin and higher in femoral catheters closed with citrate solution. Significant correlations were found between catheter tip colonization and the history of infection in group 1 (r=0.405, p=0.02), and between colonization and catheter site in group 2 (r=0.440, p=0.008).

Parameter	Group 1	Group 2
MRSA	7	4
MSSA	3	2
E. coli	0	1
K. pneumonia	1	0
P. mirabilis	0	1

Note: Group 1: Catheters closed with heparin. Group 2: Catheters closed with citrate solution. MRSA: Meticilin Resistant *S. aureus*. MSSA: Meticilin Sensitive *S. aureus*.

Table 3. Microorganisms detected in the catheters.

Factors affecting catheter colonization

No statistically significant correlations were observed between the groups when comparing the presence of diabetes, hyperlipidemia, nasal carriage, anticoagulant drug usage, and serum parameters (p>0.05). Catheter tip cultures were positive in 28.3% (n=19) of the samples. The frequency of bacterial colonization of catheters was calculated as 11.2 episodes per 1000 catheter days. To investigate factors that may affect catheter colonization, the catheters were reevaluated in two sub-groups: Reproductive and non-reproductive. The mean age of the patients in the reproductive group was 54.6 ± 18.3 years, while it was 55.0 ± 17.7 years in the non-reproductive group (p=0.926). The average duration of catheter use was 26.3 ± 28.2 days in the reproductive group and 25.1 ± 27.2 days in the non-reproductive group (p=0.872). The average total number of hemodialysis sessions with the same catheter in the reproductive group was 11.9 ± 10.6, while it was 10.5 ± 11.0 in the non-reproductive group (p=0.637). Colonization was detected in 10 femoral catheters (27.8%) and in 9 jugular catheters (29%) (p=0.534). Among patients with colonized catheters, 3 (15.8%) of them had nasal carriage, while it was detected in 2 out of 48 catheters (4.2%) that were not colonized (p=0.224). Diabetes Mellitus (DM) was present in 10 patients with positive catheter tip culture (52.6%), while 13 out of the 48 catheters without colonization (27%) were associated

with a diagnosis of DM. The presence of diabetes was significantly higher in patients with positive catheter culture (p=0.04).

Discussion

In this study, the incidence of catheter colonization was found to be 28.3%, with an occurrence rate of 11.2 episodes per 1000 catheter days. The type of catheter lock solution did not have a significant effect on the incidence of catheter colonization. However, the colonization rate was higher in jugular catheters locked with heparin and femoral catheters locked with citrate solution. The presence of infectious conditions increased the risk of catheter colonization when heparin solution was used. Additionally, patients with diabetes mellitus had a higher colonization rate. Nasal carriage did not significantly affect the catheter colonization rate.

The risk of infection in patients undergoing hemodialysis with a central venous catheter is approximately 10 times higher than in patients with arteriovenous fistulas [15,16]. Catheter-Related Bloodstream Infection (CRB) is a serious complication for hemodialysis patients, with high morbidity and mortality rates. The average incidence of CRB ranges from 3.4 to 6.5 episodes per 1000 catheter days [17-20]. Catheter colonization is a necessary step for CRB, but the exact pathogenesis is not fully understood. It is known that catheter colonization precedes catheter infection, leading to CRB.

Previous studies have reported the incidence of catheter-related bacteremia for temporary catheters to be around 15-18%, with higher rates occasionally reported. The rate of catheter colonization in these studies has ranged from 21.6%to 34.9%. In this study, catheter colonization was directly examined without evaluating the frequency of catheter-related bacteremia, and the colonization rate was found to be 28.3%, which was higher than in other published studies.

Various factors can affect catheter colonization. Previous studies have identified risk factors for catheter infection, including age over 65 years, diabetes mellitus, low serum albumin levels, nasal carriage of staphylococci, poor personal hygiene, longer duration of catheter use, and catheter placement location. In this study, nasal carriage was detected in only 7.5% of patients, and there was no significant relationship between nasal carriage and colonization rates for both catheter lock solutions. The lower nasal carriage rate in this study may explain the lack of significance.

Another risk factor for catheter colonization is the duration of catheter use. The KDOQI guidelines recommend shorter durations of stay for femoral catheters (less than 5 days) and jugular catheters (less than 3 weeks). Prolonged catheter use has been associated with increased colonization and catheter-associated bacteremia rates. In this study, the duration of catheter stay was significantly higher than recommended, which may be attributed to a lack of routine follow-up by nephrologists for a significant proportion of end-stage renal disease patients.

Catheter placement location has also been associated with colonization risk, with the subclavian vein showing the lowest risk and the femoral catheter the highest. However, the subclavian vein is not recommended due to complications, and the femoral catheter is often chosen to avoid interfering with potential fistula or graft sites. In this study, higher colonization rates were observed in jugular catheters locked with heparin and femoral catheters locked with citrate. Specifically, a significant correlation was found between femoral catheter localization and catheter colonization when citrate was used.

Diabetes mellitus is an independent risk factor for septicemia in patients with end-stage renal disease, and it has been associated with increased risk of catheter colonization and catheter-related bacteremia. Similarly, in this study, diabetes was identified as a risk factor for catheter colonization, independent of the catheter lock solution.

Strict hygiene measures, eradication of nasal carriage of *Staphylococcus aureus*, and additional methods such as topical antimicrobial agents at the catheter exit site, antibiotic-impregnated catheters, and silver-impregnated cuffed catheters are recommended to prevent catheter-related infectious complications. Intraluminal antimicrobial solutions, including sodium citrate, have been studied for their potential to inhibit biofilm formation and exhibit antimicrobial properties. However, in this study, catheter lock solutions had no significant effect on catheter colonization rates, as both groups showed similar rates of colonization.

Staphylococci were the most commonly isolated microorganisms responsible for catheter-related infections, accounting for 60% to 90% of catheter-related bacteremia cases. Coagulase-negative Staphylococcus, particularly *S. epidermidis*, was frequently isolated (35-50% of cases). *S. aureus* was the second most common isolated bacteria, responsible for 15-25% of nosocomial catheter infections. In this study, staphylococci were also the most commonly isolated bacteria, accounting for 84% of catheter tip cultures.

This study has several limitations that should be acknowledged. First, the sample size was relatively small, which may limit the generalizability of the findings. Additionally, the study was conducted at a single center, potentially introducing bias, and limiting the diversity of the patient population. Furthermore, the study relied on retrospective data collection, which may have resulted in incomplete or inaccurate information. Another limitation is that only two catheter lock solutions were compared, and other potential solutions were not included. Moreover, the study did not investigate other potential risk factors for catheter colonization, such as patient comorbidities or the presence of biofilm on catheter surfaces. Despite these limitations, the study has several strengths. It provided valuable insights into the incidence of catheter colonization and the potential impact of catheter lock solutions. The study utilized rigorous statistical analysis methods, enhancing the reliability of the results. The study also included detailed information on patient characteristics and catheter-related factors, allowing for a comprehensive examination of potential associations. Additionally, the study evaluated the presence of nasal carriage, a known risk factor for catheter-related infections. The findings of this study contribute to the existing body of knowledge on catheter colonization and provide a foundation for further research in this area.

Conclusion

In conclusion, this study found a significant incidence of catheter colonization, with higher rates observed in jugular catheters locked with heparin and femoral catheters locked with citrate. The presence of diabetes mellitus was identified as a risk factor for colonization. Catheter lock solutions did not significantly affect colonization rates. Staphylococci were the predominant microorganisms isolated from catheter tip cultures. Further efforts to prevent catheter-related infectious complications should focus on strict hygiene measures and targeted interventions based on identified risk factors.

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How to cite this article: Sakaci, Tamer, Baris Doner, Tuncay Sahutoglu and Ekrem Kara, et al. "Impact of Catheter Lock Solutions and Patient Factors on Catheter Colonization in Temporary Hemodialysis Catheters." *J Nephrol Ther* 15 (2025): 552.